

AMENDMENTS TO THE SPECIFICATION:

Page 1,

insert at the beginning:

--This application is a division of application Serial Number 10/029,259, filed December 28, 2001, which is a division of application Serial Number 08/813,842, filed March 7, 1997, now U.S. Patent No. 6,346,551, which is a continuation of international application PCT/JP95/01783, filed July 9, 1995, now abandoned.--

The paragraph beginning at page 26, line 17, has been amended as follows:

--~~Objective~~ An objective of this invention is to resolve the problems above mentioned, and to provide inhibitory or blocking agents of molecular generating and/or inducing functions, that can inhibit or block ~~function~~ functions generated by the multi-dimensional ~~structure~~ structures of reactive substrates ~~and has~~ and have a simple chemical structure.--

The paragraph beginning at page 26, line 24, has been amended as follows:

--In order to complete the above-mentioned objective, ~~as the result that the inventors repeated~~ carried out research ~~with all our mind, this invention came to be completed and determined~~ that the chemical compounds ~~which is~~ which are shown in the following general ~~formula~~ formulae (1-a), (1-b), ~~(1-b), general formula (2), general formula (3-a) and (3-b)~~ or ~~these~~ acid addition salt compounds thereof which are active provide the objective mentioned above.--

The paragraph beginning at page 140, line 5 has been amended as follows:

--DNA or RNA synthesis device (392-25 type, Perkin-Elmer Co.) was used and 7 base alignment (CTTCGGA) and (CTTCGGG) new synthesis dimer (SEQ ID NO: 1) (5'>CTTCGGACTTCGGA<3') and (SEQ ID NO: 2) (5'>CTTCGGGCTTCGGG<3') were synthesized. Then, an effect of Yoshixol on a change in molecular weight of the dimer was investigated. This pellet was dissolved on 50  $\mu$ l of

tris EDTA, and OD260 was measurement by 100 times attenuation so that concentration was turned into equality (5 ng/ $\mu$ l) by tris EDTA and distilled water. And, 4  $\mu$ l of an adjusted synthesis dimer was labeled at 5'-terminal end of the dimer with 4  $\mu$ l of ATP which was labeled by P32. In addition, after processing the dimer with 1  $\mu$ l of polynucleokinase (TaKaRa, Tokyo) for 30 minutes by 37°C, the solution was heated at 70°C for 5 minutes. Afterward, 65  $\mu$ l of tris EDTA, 1  $\mu$ l of glycogen and 190  $\mu$ l of chilled ethanol were added and were mixed. And, it was centrifuged over 10 minute by 16,000 cpm. After taking the supernatant out, the pellet was made dry. Again, it was dissolved by 50  $\mu$ l of tris EDTA and, 1  $\mu$ l of the solution with radioactivity was mixed with urea (15 g), acrylamide (5.7 g), bisacrylamide (0.3 g), tris boric acid EDTA (3 ml), 10% ammoniumpersulfate (0.1 ml) and N, N, N, N-tetramethyldiamine (15  $\mu$ l) to distilled water, so that the volume was made to 30 ml in total. Then, 20% gels were made and the electrophoresis with constant voltage of 10 watt was performed to be exposed on a film. Changes in molecular

weight with the dimers were investigated by the sample which was consisted of 2  $\mu$ l of the solution which was dissolved by final tris EDTA with 2  $\mu$ l of Yoshixol. As the control sample, 2  $\mu$ l of distilled water was added to the solution. Then, each test sample was given 6  $\mu$ l of the stop solution. Change in molecular weight of the synthesized dimers with Yoshixol did not differ from that without the treatment (referred Figure 37). Therefore, this result shows that Yoshixol does not change a distribution of molecular weights with new synthesized dimers (SEQ ID NO: 1) (5'>CTTCGGACTTCGGA<3') and (SEQ ID NO: 2) (5'>CTTCGGGCTTCGGG<3') and does not change at least a primary structure.--

The paragraph beginning at page 141, line 17 has been amended as follows:

--Effect of Yoshixol on PCR was investigated by DNA template which was extracted from snake (blue-green snake, captured at Matsumoto city, Nagano). The new synthesized dimer of (SEQ ID NO: 2) (5'>CTTCGGGCTTCGGG<3') with 7 base-

pair alignment (CTTCGGG) above-mentioned was used as a primer. PCR reaction was done by use of DNA thermal cycler (PJ-2000) made in PERKIN ELMER CETUS company. The following six combinations were prepared for the test samples. Those are two kinds of samples which consist of 5  $\mu$ l of primer (100 pico mole/ $\mu$ l) with 5  $\mu$ l of Yoshixol (P+) and without Yoshixol (P-). In addition, two kinds of samples which consist of 5  $\mu$ l of snake DNA (500 ng/ $\mu$ l) with 5  $\mu$ l of Yoshixol (D+) and without Yoshixol (D-). And, additional two kinds of samples which consist of 1  $\mu$ l of polymerase enzymes (Recombinant Taq DNA Polymerase, No. R001A, TaKaRa Shuzo Co., Otsu city: 5 unit/ $\mu$ l) with 1  $\mu$ l of Yoshixol (Pm+) and without Yoshixol (Pm-). After each sample was placed for 10 minutes at room temperature, each sample was diluted in distilled water. And, it is adjusted in a primer solution of 10 picomole/ $\mu$ l, DNA solution of 50 ng/ $\mu$ l and a polymerase enzymes solution of 0.5 unit/ $\mu$ l. Then, the following combinations were prepared. On PCR, a primer solution of 5 ml which is diluted mentioned above, 5 ml of DNA solution, 5  $\mu$ l of buffer solution for PCR

reaction, 0.25  $\mu$ l of polymerase enzymes solution and 4  $\mu$ l of dNTP mixed solution were added in distilled water to be made total volume of 50  $\mu$ l. Combination of each sample is following five groups. First, each sample is not added Yoshixol as the control (P-, D-, Pm-). Second is the sample which only a primer has processed by Yoshixol (P+, D-, Pm-). Third is the sample which only DNA has processed by Yoshixol (P-, D+, Pm-). Fourth is the sample which polymerase enzymes alone has processed by Yoshixol (P-, D-, Pm+). In addition, fifth is the sample which concentration of Yoshixol for the polymerase is increased to 100 times on P-, D-, Pm+ series above mentioned (P-, D-, Pm+A). In each combination, amount of cDNA synthesis was amplified by a PCR method and was measured. On the group of P-, D-, Pm- which all samples were not treated, 4 bounds between a molecular weight of 0.5 and 1.2kb were found. Also, the bounds in P-, D-, Pm- did not differ from those in P+, D-, Pm- and P-, D+, Pm-. But, on the group of P-, D-, Pm+, only one bound at lowest molecular weight within 4 bounds was appeared. In addition, any kind of

bounds did not observe on the group of P-, D-, Pm+A (referred Figure 38). This result shows that Yoshixol controls or inhibits functional generation of polymerase enzymes which is related to transcription and/or amplification of the base-pair alignment generated by DNA template which consists of many base-pair alignments. It is to be needless to say that inhibitory effects of molecular generating and/or inducing functions which was carried in claims 1-11 in this invention are not restricted by the primer which is new synthesized dimer (SEQ ID NO: 2) (5'>CTTCGGGCTTCGGG<3'), snake DNA and polymerase enzymes demonstrated here.--